672.26

The University of Chicago
FOUNDED BY JOHN D. ROCKEFELLER

Condensations with Benzoin by means of Sodium Ethylate

A DISSERTATION PRESENTED TO THE FACULTY OF ARTS, LITERATURE, AND SCIENCE OF THE UNIVERSITY OF CHICAGO, IN CANDIDACY FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

By JAMES BERT GARNER

STANFORD UNIVERSITY LIBRARIES
WITHDRAWN

CHICAGO
The University of Chicago Press
1897

3781
C53G
UNCLASSED

The University of Chicago
FOUNDED BY JOHN D. ROCKEFELLER

Condensations with Benzoin by means of Sodium Ethylate

A DISSERTATION PRESENTED TO THE FACULTY OF ARTS, LITERATURE, AND SCIENCE OF THE UNIVERSITY OF CHICAGO, IN CANDIDACY FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

By JAMES BERT GARNER

CHICAGO
The University of Chicago Press
1897

CONDENSATIONS WITH BENZOIN BY MEANS OF SODIUM ETHYLATE.

When benzoin and sodium ethylate are brought together in absolute alcohol under the conditions described below a crystalline product appears. This body had apparently been noticed by Victor Meyer[1], but was not investigated by him. It is probably an additive product of the formula—$C_{16}H_{17}O_3Na$, with some alcohol of crystallization—and it was thought that an examination of its properties and reactions would be of interest. Two classes of reactions were studied: (1) the behavior of the compound towards ordinary reagents; and (2) reactions in which by its means benzoin is added to unsaturated aldehydes and ketones. The work was also extended to include the behavior of benzfuroin and cuminoin under similar circumstances.

I. SODIUM ETHYLATE ADDITION PRODUCT OF BENZOIN.

1. BENZOIN WITH SODIUM ETHYLATE AT 25°.

One molecule (5 gr.) of carefully purified benzoin of melting point 134° was dissolved in absolute ethyl alcohol (75 cc.) and allowed to cool to about 25°; then a solution of one atom of sodium (.6 gr.) in absolute ethyl alcohol (75 cc.) was added. The mixture immediately became deep red, and in a few minutes the whole solidified to a mass of long white silky needles. By filtering rapidly and washing well with absolute alcohol and absolute ether and transferring to a vacuum desiccator the inevitable decomposition, due to the action of moist air, was for the most part avoided. After drying for one-half hour over concentrated sulphuric acid in vacuo the following analyses were obtained:

I. 0.8081 grs. gave 0.1302 grs. Na_2SO_4.
II. 0.4522 " " 0.0737 " " .

Found	I.	II.
Na =	5.22	5.27

No satisfactory analysis for carbon and hydrogen could be obtained —due, probably, to the fact that the amount of alcohol of crystallization was not constant.

[1] Victor Meyer and V. Päpcke, Ber. *21*, 1335.

The product is decomposed[2] by all the ordinary solvents, including water; the products being benzoin, alcohol, and sodium hydroxide. It appears to be stable only in the presence of excess of absolute alcohol and in the absence of moisture. On long exposure to air benzoin, sodium benzoate, and alcohol are the products of decomposition.

The reactions described below indicate that the sodium ethylate has been added to the carbonyl group:

$$\begin{array}{l} C_6H_5 \cdot CH\,OH \\ C_6H_5 \cdot C{<}\begin{array}{l} O\,Na \\ OC_2H_5 \end{array} \end{array} .$$

Although similar products in the case of aldehydes, esters, and ketones have not been isolated and analyzed, their formation has been assumed, *e. g.*, in all instances of the "aldol condensation" where sodium ethylate is the condensing agent. In one particular case, viz., that of benzoic ether, Claisen[3] has isolated the addition product, which he has conclusively proved to be

$$C_6H_5 - C{<}\begin{array}{l} ONa \\ OC_2H_5 \\ OC_2H_5 \end{array} .$$

The constitution of the benzoin addition product is shown by its deportment with benzyl chloride in the formation of

Benzyloxyethoxybenzoin.

$$\begin{array}{l} C_6H_5 - CH\,OH \\ C_6H_5 - C{<}\begin{array}{l} O\,CH_2 \cdot C_6H_5 \\ O\,C_2H_5 \end{array} \end{array} .$$

This is best prepared as follows: One molecule of benzoin (5 gr.) dissolved in absolute ethyl alcohol (75 cc.) was treated with a solution of one atom of sodium (.6 gr.) in absolute ethyl alcohol (75 cc.), the mass allowed to solidify, and to the whole was added one molecule of benzyl chloride (4 gr.). After boiling in a water bath for thirty minutes, using a reflux condenser, the mixture became yellow and a white solid separated, which was identified as sodium chloride. On standing for twelve hours at 0° nothing else appeared; the salt was filtered off and the alcohol removed by distillation at 25 mm. in the

[2] Jackson, Amer. Chem. Jour. *XVII*, 601.

[3] Claisen, Ber. *20*, 653.

water bath. The semi-solid mass remaining was treated with cold water and was found to be neutral to litmus paper. By extracting with ether and shaking with sodium carbonate and caustic soda a neutral heavy yellow oil remained, which on fractionation in vacuo yielded benzyl ether (B. P. 78° at 25 mm.) and benzyloxyethoxybenzoin (B. P. 199° at 25 mm.). The latter fraction on cooling solidified, and after recrystallization from ligroin (B. P. 110–120°) melted at 110–112°. On analysis:

0.2004 grs. gave 0.5895 grs. CO_2 and 0.1325 grs. H_2O.

Found:	Calculated for $C_{23}H_{24}O_3$.
C = 80.18	79.31
H = 7.34	6.89

The figures obtained are somewhat high, but in all probability this is due to traces of ligroin, from which the substance was recrystallized. These last traces could not be removed without decomposing the substance. No other solvent was found which would give crystals equally pure. It is easily soluble in cold ether, benzene, alcohol, acetic ether, and chloroform.

Its behavior towards reagents sufficiently establishes its constitution. In recrystallizing from high boiling ligroin it suffers partial decomposition, and by continued boiling with this reagent it can be completely decomposed into benzoin and benzyl ether. The presence of the CHOH group is shown by the fact that the substance reduces Fehling's solution. If differs from benzoin in exhibiting this reaction instantly in the cold. The hydroxyl group in benzoin reacts slowly and with some difficulty with acetyl chloride. The preparation of acetylbenzoin requires boiling with acetyl chloride and glacial acetic acid for one-half hour. The hydroxyl group in benzyloxyethoxybenzoin reacts, on the other hand, vigorously in the cold with

Acetyl Chloride.

When one molecule of the substance, dissolved in glacial acetic acid, is treated with five molecules of acetyl chloride, there is a sudden evolution of hydrochloric acid gas. The reaction is complete in ten minutes. The resulting compound, however, appears to be unstable even at low temperatures, and is decomposed quantitatively into acetylbenzoin and benzyl ether. The acetylbenzoin was identified by a comparison with acetylbenzoin made from benzoin and acetic anhy-

dride. In addition to the above differences benzyloxyethoxybenzoin is distinguished readily from benzoin by its giving at first a blood-red coloration with cold concentrated sulphuric acid, which afterward changes to yellow.

2. BENZOIN WITH SODIUM ETHYLATE AT 90°.

The only systematic attempt to determine the action of sodium ethylate or caustic potash on benzoin in boiling alcohol seems to have been made by Jena and Limpricht.[4] But their experiments being all made with 92 per cent. alcohol, the results obtained by them could not be expected to be comparable with those obtained by the use of pure sodium ethylate in absolute alcoholic solution. In all experiments below 170°, but with varying concentrations, some in presence and some in absence of much air, they found practically the same products.

Hydrobenzoin,	Aethylbenzilic acid [doubtful],
Aethylbenzoin,	Benzoic acid; only traces in
Benzoin pinakon [?],	absence of air.

By the distillation of "benzoin pinakon" with dilute sulphuric acid, they obtain two substances, one of which, melting at 190° and not further investigated, is probably identical with the keto-lactone ($C_{16}H_{14}O_2$) described below. The presence of water in their experiments renders it difficult to interpret their results, and to determine the precise nature of the reactions. In the present work, the confusion, introduced by the presence of water, was avoided by the use of absolute alcohol in every experiment. The same relative concentrations were always employed, and the effects of different temperatures, and the presence or absence of much air ascertained. The experiments were all conducted in diffused light; the flask was sunk completely in the water bath and covered with several layers of thick toweling so that the acceleration in the oxidation of benzaldehyde observed by Schönbien[5] could not have appreciably affected the results of these experiments.

If the sodium ethylate addition product of benzoin is suspended in absolute alcohol and heated in a water bath for some time, it gradually goes into solution in consequence of a complicated chemical action. In order to obtain products, free from tar, and a complete reaction, the following proportions must be strictly adhered to, and the described

[4] Jena and Limpricht, Ann. *155*, 94.

[5] Schönbein, Ann. *102*, 129; Jour. f. prakt. Chemie *75*, 73.

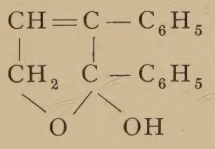
conditions complied with: To a solution of one molecule of benzoin (15 grs.) in absolute ethyl alcohol (225 cc.) was added a solution of one molecule of sodium (1.8 grs.) in absolute ethyl alcohol (175 cc.). The mixture was allowed to solidify and then was boiled in a water bath for twenty-six hours, using a reflux condenser. During the boiling the mixture changed in color from a deep red to a pale yellow, and all the solid went into solution. The end of the reaction is not reached until these conditions have been realized. The alcohol was *completely* distilled off and the yellow solid remaining was thoroughly digested with 500 cc. of cold water. The insoluble portion was filtered off and proved to be a mixture of hydrobenzoin (95 per cent.) and isohydrobenzoin (5 per cent.) The filtrate was strongly alkaline. It was extracted twice with ether and the extract dried with calcium chloride. On removing the ether, the residue was found to be hydrobenzoin. On acidifying the cold alkaline solution with dilute sulphuric acid a copious white precipitate was formed. The product was agitated twice with ether and the ethereal extract was shaken with sodium carbonate and then with caustic soda. By adding dilute sulphuric acid to the carbonate solution, a white precipitate was obtained which consisted of benzoic acid and a substance ($C_{16}H_{14}O_2$) melting at 195°, and subsequently shown to be lactonic in character. From the caustic soda solution, more benzoic acid and an acid melting at 174.5° were obtained. From fifteen grams of benzoin by the above reaction there were obtained in a typical case:

Keto-lactone, - -	5.6 grs.	Acid (M. P. 174.5°), -	0.17 grs.
Hydrobenzoin, -	5.4 "	Benzoic acid, - -	2.6 "
Isohydrobenzoin, -	0.25 "		

The hydrobenzoin was identified by its solubilities, crystalline form, melting point; its oxidation to benzoin and benzil by nitric acid; and the formation of the characteristic diacetate.

The benzoic acid was identified by its melting point, solubilities, crystalline form, sublimation at 100°; and its conversion into benzoic ether.

Keto-lactone.



The substance melting at 195° was separated from benzoic acid by boiling with water, in which it is insoluble, and filtered through a hot water funnel. After two recrystallizations from a mixture of alcohol and ligroin (B. P. 40-60°), crystals in large plates were obtained. On analysis and molecular weight determination figures were obtained agreeing with formula $C_{16}H_{14}O_2$.

I. 0.1976 grs. gave 0.5839 grs. CO_2 and 0.1126 grs. H_2O.
II. 0.2072 " " 0.6122 " CO_2 and 0.1162 " H_2O.

Found:	I	II	Calculated for $C_{16}H_{14}O_2$:
C =	80.60	80.58	80.64
H =	6.33	6.23	5.88

Molecular weight determinations by boiling point method with glacial acetic acid as solvent were as follows:

I. 0.1288 grs. gave an elevation of 0.054° in 25.30 grs. solvent
II. 0.1050 " " " " 0.049° in 25.30 " "

Found:	I	II	Calculated for $C_{16}H_{14}O_2$:
	238.	225.	238.

The substance is insoluble in sodium carbonate, cold caustic soda, and hot ligroin (B. P. 40–60°). It is soluble in hot benzene, ligroin (B. P. 110–120°), ether, alcohol, acetic acid and cold chloroform. With concentrated sulphuric acid, it gives a deep yellow color, which changes to deep red in warming. It is soluble in alcoholic solutions of potash, sodium hydrate, and barium hydrate.

Phenylhydrazine, hydroxylamine, bromine in chloroform solution, and concentrated hydrochloric acid (in sealed tubes at 200°) do not interact with it. Chromic acid oxidies it to benzoic acid and carbon dioxide. The neutral substance has all the properties of a γ-lactone and is comparable in its chemical deportment with the lactones obtained by Fittig and Young.[6]

Oxidation of the Keto-lactone.

Since the keto-lactone showed but few reactions, it was deemed advisable to determine the behavior towards reagents of the keto-alcohol, from which the keto-lactone was obtained. If reference is made to the preparation of the keto lactone, it will be observed that after boiling the benzoin with sodium ethylate in the water-bath for twenty-

[6] Fittig and Young, Ann. *216*, 38.

six hours, and the removal of the alcohol and hydrobenzoin, an alkaline filtrate is left from which the keto-lactone can be obtained by acidification. If this alkaline filtrate is treated in the cold with the calculated amount of potassium permanganate, the latter is instantly decolorized. On examination of the products, it is found that the keto-alcohol has suffered a loss of two hydrogen atoms only, and that the resulting substance has the empirical formula $C_{16}H_{12}O_2$. It is separated from benzoic acid, with which it is mixed by boiling with water. When pure, it melts at 138.5°. The substance is easily separated from the keto-lactone by its ready solubility in 95 per cent. alcohol at 65°, whereas the keto-lactone is almost insoluble. On analysis :

0.1924 grs. gave 0.5650 grs. CO_2 and 0.0922 grs. H_2O.

Found	Calculated for $C_{16}H_{12}O_2$:
C = 80.09	81.35
H = 5.32	5.08

The substance is soluble in hot alcohol, acetic ether, benzene, and chloroform, and almost insoluble in hot ligroin (B. P. 40–60°). No interaction takes place between this substance and phenylhydrazine, hydroxylamine, acetyl chloride, acetic anhydride, bromine, or alcoholic ammonia (in sealed tubes at 200°).

Saponification of Keto-lactone.

By boiling the keto-lactone for one hour on a reflux condenser with four molecules of alcoholic potash, a clear solution is obtained, which leaves, on evaporation of the alcohol, a reddish solid, easily soluble in cold water. By acidifying this solution in the cold, an acidlike substance is obtained, melting at 174.5°, but if the solution is acidified at 15°, a mixture of this with the keto-lactone is precipitated. The acidlike substance on standing readily changes into the keto-lactone body, and is therefore related to it as an acid to its lactone. A silver salt of the acidlike substance was prepared, but it, too, on treatment with warm water, suffered decomposition into silver oxide and the keto-lactone. Attempts were made to prepare barium and calcium salts, but neither could be obtained pure enough for analysis.

Acetyl Derivative of the Keto-lactone.

If the substance is boiled, using a reflux condenser, with a mixture of acetic anhydride and anhydrous sodium acetate for two hours, the

whole poured into water, and the solid, which separates, recrystallized repeatedly from alcohol, large transparent plates, melting at 144°, are formed. By careful drying at 100°, and analyzing, figures were obtained showing it to be a monoacetyl derivative.

0.1945 grs. gave 0.5516 grs. CO_2 and 0.1033 grs. H_2O.

Found:	Calculated for $C_{18}H_{16}O_3$
C = 77.34	77.14
H = 5.90	5.71

It is soluble in cold benzene, ether, acetic ether and hot alcohol and acetic acid; insoluble in hot ligroin (B. P. 40–60°). By saponification with alcoholic potash, it is reconverted into the original substance. With concentrated sulphuric acid it gives a deep red color.

Fusion with Caustic Potash.

By fusing with solid caustic potash the lactone is converted into benzoic acid (3 parts) and cinnamic acid (1 part) with some acetic acid. The fusion is best carried out as follows: Three grams of finely powdered substance are gradually added to a fused mass of 30 grs. of caustic potash at 200°, and thoroughly stirred in. After maintaining this temperature for 10 minutes the mass becomes yellow, and the odor of benzoic acid is perceptible. The mass is allowed to cool, then dissolved in cold water. Any unchanged substance is filtered off, and the filtrate acidified with dilute hydrochloric acid. The mixture is extracted with ether and the extract shaken with sodium carbonate and caustic soda in turn, and the ether evaporated to recover any lactone which may have been formed during the acidification. By acidifying the carbonate solution and extracting with ether, the mixture of benzoic and cinnamic acids is obtained. The two acids are separated by sublimation in the water bath, or by their relative solubilities in ligroin (B. P. 40–60°). The acids are identified by their esters, solubilities, melting points, etc. The cinnamic acid is farther identified by the analysis of its barium salt.

0.1339 grs. gave 0.0674 grs. $BaSO_4$.

Found:	Calculated for $C_{18}H_{14}O_4Ba \cdot 2H_2O$:
Ba = 29.57	Ba = 29.33.

Primary Reaction—Formation of Keto-lactone.

It is clear from the above results that two reactions must have taken place side by side. The primary reaction consisted in the formation

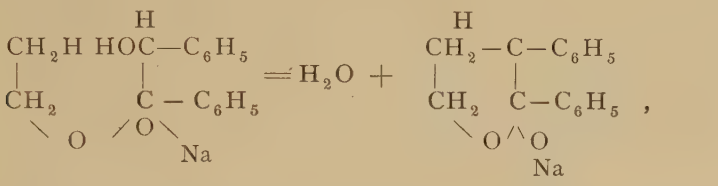
of a keto-lactone and hydrobenzoin in molecular proportions according to the following equation :

$$2C_{14}H_{12}O_2 + C_2H_5OH = \underset{\text{Hydrobenzoin}}{C_{14}H_{14}O_2} + \underset{\text{Keto-lactone}}{C_{16}H_{14}O_2} + H_2O.$$

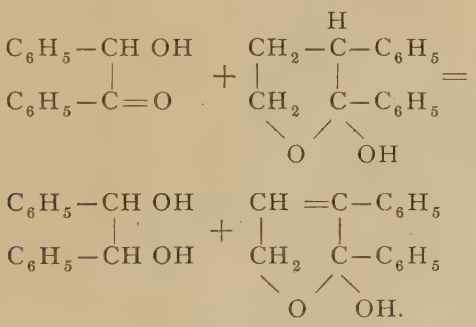
It is, therefore, but for the intervention of alcohol and the elimination of water, precisely parallel to the conversion of benzaldehyde by alkalies into benzyl alcohol and benzoic acid.

$$2C_7H_6O + H_2O = C_7H_8O + C_7H_6O_2.$$

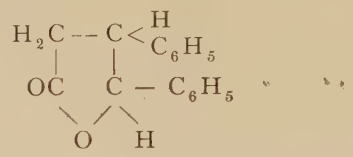
The mechanism of this reaction seems to be that the sodium ethylate addition product, at the boiling point of alcohol, partly dissociates, yielding benzoin, while the undissociated product loses the elements of water as follows :



which is subsequently oxidized by the benzoin in the following manner, yielding the lactone and hydrobenzoin in molecular proportions.



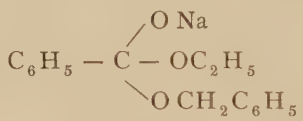
The formation of an acetyl derivative, the opening of the ring by alcoholic potash to form a substance with acid properties, which passes back into the lactone with extreme ease, the oxidation to benzoic acid and carbon dioxide with chromic acid, the splitting, by fusion with caustic potash, into benzoic and cinnamic acids, with some acetic acid, and the mode of formation support this view of the constitution. The formula



might possibly account for the reaction, although the formation of a body with this formula could not be explained without the assumption of an internal rearrangement of a somewhat unusual character. A substance with this constitution, however, is already known,[7] and differs markedly in its properties from the present substance.

Secondary Reaction.

Parallel with the above reaction, a splitting of benzoin into benzaldehyde takes place to an extent varying with the temperature and the presence or absence of much air. The conversion of benzoin into benzaldehyde seems to have been noticed in but two other occasions, viz., by Zinin[8] and Michael and Palmer.[9] The methods employed by them involved the use of high temperatures. Claisen[10] has shown that when benzaldehyde is treated with sodium ethylate, under conditions different from those above described, a substance of the constitution



is formed. When it is treated with water it decomposes into benzyl alcohol and sodium benzoate, while with acetic acid it yields benzyl alcohol, benzyl benzoate and benzoic ether. A secondary reaction of sodium ethylate on benzaldehyde, such as the above, could not have taken place here, as there is not formed a trace of benzyl alcohol, benzyl benzoate, or benzoic ether.

It was important to ascertain whether the two reactions were independent, and, if so, what would be the conditions necessary for the completion of the one and the exclusion of the other. It was found that in the cold and in absence of air, benzoin, treated with one molecule of sodium ethylate, simply forms the crystalline addition product

[7] Japp and Landers, Jour. Chem. Soc. *1897*, 154.

[8] Zinin, Ber. *6*, 1207.

[9] Michael and Palmer, Amer. Chem. Jour. *VI*, 98.

[10] Claisen, Ber. *20*, 646.

which is unchanged after standing for three weeks. In the cold, even in presence of air, no keto-lactone is found.

On the other hand, benzoin, treated with one molecule of sodium ethylate in presence of air at 90°, undergoes the primary reaction to the extent of four-fifths, and the remaining one-fifth is converted into benzoic acid, this product arising from the oxidation of the benzaldehyde by the air in presence of the excess of alkali. It therefore seemed advisable to make experiments at higher temperatures, the other conditions remaining the same.

3. BENZOIN WITH SODIUM ETHYLATE AT 100°.

To one molecule of benzoin (4 gr.) dissolved in absolute ethyl alcohol (60 cc.) in a sealing tube was added a solution of one atom of sodium (.42 gr.) in absolute ethyl alcohol (45 cc.). The mass was allowed to solidify, then the tube sealed. The mixture was heated at 100° for fifteen hours, or until all of the solid was in solution. When the tube was opened no pressure was found. The excess of alcohol was distilled off in a water bath, and the following products were obtained:

Keto-lactone, 2.	Benzoic acid, 0.2.
Hydrobenzoin, 1.8.	Benzoin (unchanged), 0.3.

From these results it is evident that the primary reaction took place *almost* entirely.

4. BENZOIN WITH SODIUM ETHYLATE AT 120–130°.

In sealed tubes at 120–130° for ten hours, a mixture prepared exactly as above gave quite satisfactory results. On careful examination of the products, the keto-lactone and hydrobenzoin were found to have been formed quantitatively.

Keto lactone, 2.3.
Hydrobenzoin, 2.0.
Benzoic acid, trace.

These results also indicate that the speed of the reaction and its direction are functions of the temperature. At 90°, as was shown above, two reactions were taking place side by side—a primary reaction to the extent of 80 per cent., and a secondary one to the extent of 20 per cent.; the time was twenty-six hours. At 100°, the primary reaction products had increased to 95 per cent., and the secondary ones

decreased to 5 per cent.; the time was fifteen hours. The quantitative completion of the primary reaction was effected at 120–130° in the brief time of ten hours. With a view of ascertaining the effect of less than a molecule of sodium ethylate on the course of the reaction the following experiment was tried.

5. BENZOIN WITH ONE-HALF MOLECULE OF SODIUM ETHYLATE AT 90°.

One molecule of pure benzoin (15 grs.) dissolved in absolute alcohol (225 cc.) was treated with one-half atom of sodium (.9 gr.) dissolved in absolute alcohol (100 cc.). The mixture, after solidification, was heated in the water bath for twenty hours, or until the solid passed into solution. The odor of benzaldehyde was prominent. The excess of alcohol was removed by distillation, and the same methods of separation employed as above in (2). The reaction products were as follows:

Keto-lactone, 2.7.	Benzoic acid, 1.4.
Hydrobenzoin, 2.2.	Benzoin (unchanged), 6.1.
Benzaldehyde, 1.9.	

These results indicate conclusively that two reactions are going on simultaneously: (1) the formation of keto-lactone and hydrobenzoin; (2) the splitting of benzoin into benzaldehyde. More than one-third of the benzoin is unchanged. The primary reaction takes place to a much smaller extent than before, and the secondary reaction to a greater extent. The product of the secondary reaction is for the greater part *benzaldehyde*, still unoxidized. This experiment not only confirms the theory of the secondary reaction, but rigidly establishes that in the experiments with one molecule of sodium ethylate, benzaldehyde is an intermediate product. The survival of the benzaldehyde in those experiments is rendered impossible by its easy transformation into benzoic acid in the presence of the greater amount of alkali and the absence of unchanged benzoin. If reference is made to the results of the experiments, with one-half molecule of sodium ethylate and, with sodium methylate below, it will be seen that the amounts of benzaldehyde isolated are almost directly proportional to the amounts of unchanged benzoin.

6. ACTION OF SODIUM METHYLATE.

In order to find out whether analogous compounds could be obtained from benzoin by the use of sodium methylate, the following experiments were tried:

1. One molecule of benzoin (15 grs.) was dissolved in absolute methyl alcohol (free from acetone) (225 cc.), and to this was added a solution of one atom of sodium (1.8 grs.) in absolute methyl alcohol (175 cc.). There was only a slight change in color. Nothing analogous to the crystalline addition product with sodium ethylate separated.

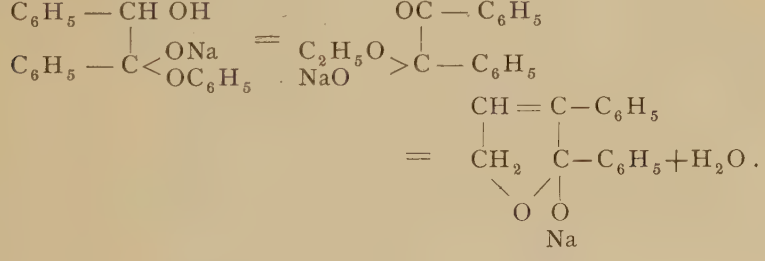
2. Another mixture, prepared as above, was boiled for twenty-six hours in a water bath, using a reflux condenser. The alcohol was distilled off in a water bath, and the yellow residue resulting was digested with 500 cc of cold water. The insoluble portion was removed by filtration and identified as benzoin. The alkaline filtrate was extracted with ether to remove any trace of benzoin or other neutral substances. Upon evaporation of the ether extract the residue was found to be benzaldehyde. From the alkaline solution nothing but benzoic acid was obtained.

Benzaldehyde, 2.5.
Benzoic acid, 1.
Benzoin (unchanged), 11.

As the results indicate, more than two-thirds of the benzoin is unchanged, and the reaction which has taken place is analogous to the secondary reaction in the sodium ethylate experiments. There is no reaction analogous to the primary reaction above, and consequently no product corresponding to the keto-lactone has been formed. This result was in accordance with the theory that the formation of a fur-furane derivative demanded an alcohol with a chain of two carbon atoms at least.

7. EXPERIMENTS WITH BENZIL.

Reverting to the theory of the mechanism of the primary reaction, another view is possible. The formation of the keto-lactone might be conceived of by the assumption of the intermediate formation of a benzil-sodium ethylate addition product, by the oxidation of the benzoin-sodium ethylate addition product. The benzil product then by loss of water would give the keto-lactone



This view was less probable since benzil forms no stable addition product with sodium ethylate, and is easily converted by alkalies into benzilic acid. On putting this theory to the test of experiment, as was anticipated, sodium ethylate and benzil under the usual conditions of concentration, gave benzilic acid, benzoic acid, and unchanged benzil as the only products. Not a *trace* of keto-lactone was formed.

II. ADDITION REACTIONS BY MEANS OF SODIUM ETHYLATE.

The following study of the second general class of reactions, effected by means of sodium ethylate, includes the investigation of the deportment of benzoin, and also of benzfuroin and cuminoin with benzalacetone, cinnamic aldehyde, cinnamic ether, and benzalacetophenone. The aim has been twofold: (1) To determine in what manner benzoin (or benzfuroin, or cuminoin,) is added to the above unsaturated substances; whether the addition is affected by a transfer either of the .H or of the .OH in the: CHOH group exclusively, or by both transfers side by side. On the assumption that the .H in the: CHOH group is transferred exclusively, formula I below would represent the constitution of the addition product (in which X may be CH_3, H, OC_2H_5, or C_6H_5); and on the other hand, if the .OH is transferred exclusively, formula II, isomeric with I, would be the type; while if both are transferred side by side, both isomers would be expected.

I. II.

$C_6H_5-CH.CH_2.CO-X$ $C_6H_5-CH-CH\,OH-CO-X$

$C_6H_5-C(OH)-CO-C_6H_5$. $C_6H_5-CH-CO-C_6H_5$.

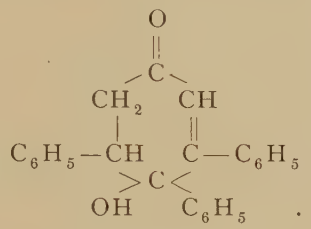
(2) To determine the influence of the group X (CH_3, H, OC_2H_5, C_6H_5), on the addition and the nature of the products formed. In any case, 1.5 diketones, as above, would be expected, but their formation and remaining as such would be conditioned by the character of the group X. Where X is CH_3, ring formation would, under the proper conditions, take place, giving rise to Δ_2 Keto-R-Hexen derivatives. On the other hand where X is H, OC_2H_5, or C_6H_5, no ring formation could take place. Knoevenagel[11] has shown that desoxybenzoin adds itself to benzalacetylacetone forming a 1.5 diketone which loses water and forms the Δ_2 Keto-R-Hexen derivative. Desoxybenzoin by a similar reaction, adds itself to benzalacetophenone forming a 1.5 diketone. These two reactions illustrate the formation of 1.5

[11] Knoevenagel, Ann. *281*, 25.

diketones by addition and their difference in behavior when X is CH_3 and C_6H_5 respectively.

I. BENZOIN AND BENZALACETONE.[12]

Under conditions described below, benzoin adds itself to benzalacetone forming



It can easily be prepared as follows: To one molecule of benzoin (6 grs.) and one molecule of benzalacetone (4.1 grs.), dissolved in absolute ethyl alcohol (100 cc.), were added a solution of sodium ethylate (4 cc.), containing one molecule of sodium (.5 grs.) in absolute alcohol (30 cc.) The mixture immediately turned deep red and on standing deposited rosettes of white needles, which after recrystallization three times from glacial acetic acid melted at 248°. The yield is about 90 per cent. of the theoretical.

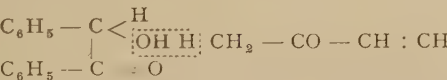
Analysis:

I. 0.1976 grs. gave 0.6126 grs. CO_2 and 0.1124 grs. H_2O

II. 0.2104 grs. gave 0.6490 grs. CO and 0.1244 grs. H_2O

Found:	I.	II.	Calculated for $C_{24}H_{20}O_2$:
C =	84.64	84.13	84.70
H =	6.27	6.57	5.88

[12] Some years ago (Ber. 26, 65), in connection with an investigation of the powers of potassium cyanide as a condensing agent, I found that when benzoin, acetone and alcohol were heated in a sealed tube with a small quantity of this reagent, a substance having the formula $C_{24}H_{20}O_2$ was the chief product. The constitution then given is fully confirmed by the results of the present work. The course of the reaction suggested was (1) the splitting of a part of the benzoin, (2) the condensation of the resulting benzaldehyde with acetone to form benzalacetone, and (3) interaction of the latter with benzoin to form



followed by (4) ring formation. Soon after, it occurred to me that the third stage might have consisted in an addition of benzoin to the double bond and subsequent ring for-

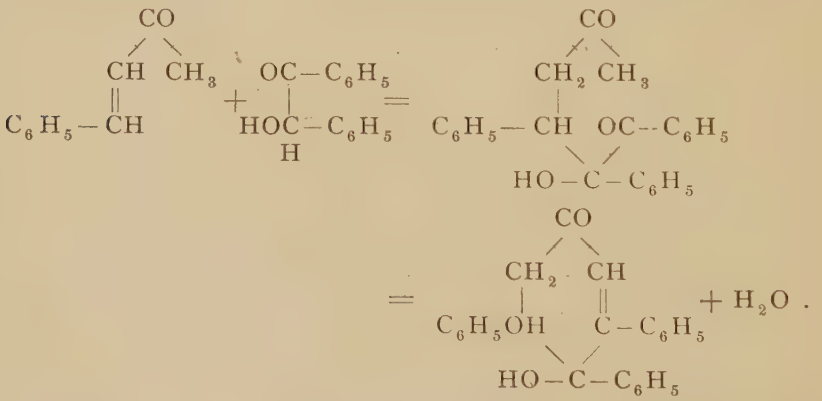
A molecular weight determination by the boiling point method, using benzene as the solvent confirmed the above formula. The benzene, used in these and following determinations, was redistilled and its constant (2670) determined by means of pure naphthalene.

0.1074 grs. gave an elevation of .031° in 28.64 grs. of solvent.
0.1296 grs. gave an elevation of .036° in 28.64 grs. of solvent.

Found :	I.	II.	Calculated for $C_{24}H_{20}O_2$
	321.	332.	340.

The substance is soluble in hot toluene, chloroform, benzene, and carbon tetrachloride; insoluble in ligroin (B. P. 40–60°). As the substance was shown to be identical with that investigated formerly by Dr. Alexander Smith, there is no need of a description of its derivatives. It is sufficient to state that the monoxim, triphenylphenol, and its acetate, were prepared and analyzed and their identity established. By the above method a larger yield of the Δ_2 Keto-R-Hexen derivative can be obtained than by the use of potassium cyanide as condensing reagent. The few details given above, such as molecular weight determination and solubilities are additional to these already published by Dr. Smith[13].

The formation of the Δ_2 Keto-R-Hexen derivative is easily understood by the assumption of the transfer of the H in the : CHOH group.



mation, giving the same final product; this would bring the action somewhat in line with the addition reactions of Michael and Knoevenagel, a ketol .CH (OH). CO. taking the place of substances containing the group .CH_2 CO. Mr. Garner's experiments show that this belief was well founded and supply a much more rapid and convenient method of preparing the substance.—A. Smith.

[13] A. Smith, Ber. *26*, 65.

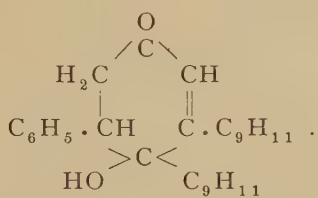
2. ACTION OF SODIUM ETHYLATE ON BENZFUROIN AND BENZALACETONE.

One molecule of pure benzfuroin (4 grs.) and one molecule of benzalacetone (3 grs.) dissolved in absolute alcohol (60 cc.), were treated with a solution (.5 gr. sodium in 30 cc. of alcohol) of sodium ethylate (2 cc.) at about 25°. The mass turned deep green. On standing for 14 hours, crystals separated which, after repeated recrystallization from glacial acetic acid, showed the constant melting point 248°. On analysis and molecular weight determination, figures were obtained entirely different from those calculated for the additive compound of benzfuroin and benzalacetone, but entirely in harmony with those of the benzoin addition product described above. The substances possessed the same solubilities, crystalline form, etc. The oxim, acetate, and phenol made from each were identical. The yield is only 27 per cent. as compared with 90 per cent. in the case of benzoin. The formation of the same product can be explained only on the assumption of the splitting of benzfuroin into benzaldehyde and furfurol, the formation of benzoin from the benzaldehyde, and then its addition to benzalacetone. This assumption is supported by the presence of furfurol alkali resin in the mother liquors, and also by the fact that furoin will not undergo the addition reaction at all. This shows that benzaldehyde can form benzoin under the same conditions where benzoin gives benzaldehyde. Benzoin as fast as it is formed is removed from the sphere of action in the formation of the Δ_2 Keto-R-Hexen derivative.

3. ADDITION OF CUMINOIN TO BENZALACETONE.

Cuminoin and benzalacetone under the influence of sodium ethylate interact and form

3-4-dicumyl-5-phenyl-4-oxy Δ_2 *Keto-R-Hexen.*



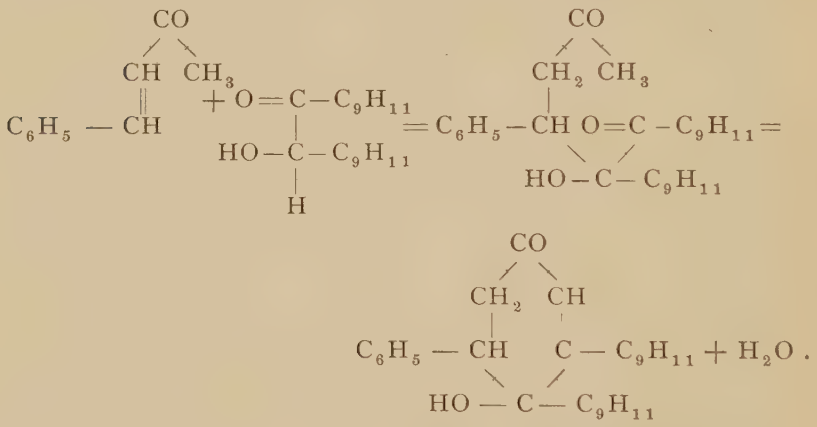
The substance is best prepared as follows: One molecule of pure cuminoin (6 grs.) and one molecule of pure benzalacetone (3 grs.), dissolved in absolute alcohol (60 cc.), are treated with a solution (6 cc.) containing .5 gr. of sodium in 30 cc. of absolute alcohol. On the

addition of the sodium ethylate the mixture turns deep red, and on standing for six hours, clusters of needles separate. By recrystallizing twice from glacial acetic acid, the pure substance, melting at 214°, can be obtained. On analysis it was found to give figures agreeing with the formula, $C_{30}H_{32}O_2$.

0.2130 grs. gave 0.6616 grs. CO_2 and 0.1562 grs. H_2O

Found :	Calculated for $C_{30}H_{32}O_2$
C = 84.77	84.90
H = 7.83	7.54.

The reaction had taken place according to the equation :



The substance is soluble in cold acetic ether, chloroform, hot benzene, and ligroin (B. P. 110–120°); insoluble in cold alcohol, ligroin (B. P. 40–60°), and hot ether. The yield is about 27 per cent. of the theoretical.

Oxim of Δ_2 *Keto-R-Hexen Derivative.*—$C_{30}H_{32}O : NOH$.

A molecule of the substance dissolved in alcohol, was boiled with three molecules of hydroxylamine hydrochloride for an hour. On cooling, nothing appeared, but after the larger portion of the alcohol had been distilled off in the water bath a solid separated, which on being well washed with water and recrystallized from a mixture of benzene and ligroin (B. P. 40–60) gave fine white needles melting at 208°. It may be recrystallized also from aqueous alcohol. The analysis shows it to be the monoxium.

0.1823 grs. gave 5.25 cc. of Nitrogen measured at 20° and 742.8mm

Found :	Calculated for $C_{30}H_{33}O_2N$
N = 3.30	3.11

The substance is easily soluble in cold acetic acid, benzene, and acetic ether : insoluble in ligroin (B. P. 40–60°).

3-4-Dicumyl-5-phenyl-phenol acetate $C_{30}H_{29}O.COCH_3$

This body can easily be prepared by boiling the Δ_2 Keto-R-Hexen derivative with a mixture of acetic anhydride and anhydrous sodium acetate for forty-five minutes, or until the mixture becomes decidedly pink in color. The solution is then poured into a large amount of cold water and allowed to settle. After recrystallization from glacial acetic acid, it is obtained in large bunches of long radiating fibers, and melts, when pure, at 122°. It is soluble in cold benzene, chloroform, ether, and ligroin (B. P. 40–60°), in hot alcohol and acetic acid.

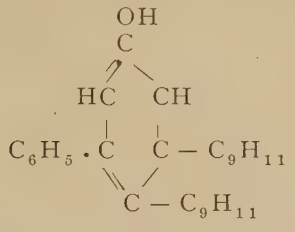
Analysis :

0.1840 grs. gave 0.5777 grs. CO_2 and 0.1245 grs. H_2O.

Found :	Calculated for $C_{32}H_{32}O_2$:
C = 85.60	85.71
H = 7.55	7.14

The acetyl derivative, when hydrolyzed by means of alcoholic potash yields

3-4-Di-Cumyl-5-Phenyl Phenol.



By warming the acetate in a water bath for ten minutes with four molecules of alcoholic potash and pouring into dilute hydrochloric acid, an amorphous mass is obtained which crystallizes from warm alcohol in large thin plates, melting at 137°. This substance is soluble in cold acetic ether, benzene, chloroform, ether and hot ligroin (B. P. 40–60°), insoluble in caustic soda.

Analysis:

0.1688 grs. gave 0.5463 grs. CO_2 and 0.1215 grs. H_2O.

Found:	Calculated for $C_{30}H_{30}O$:
C = 88.26	88.66
H = 7.99	7.39

The formation of the above substances is precisely parallel to the formation of similar substances from benzoin and benzalacetone.

4. ADDITION OF BENZOIN TO CINNAMIC ALDEHYDE.

The application of the above reaction to a mixture of benzoin and cinnamic aldehyde resulted in the formation of

Benzoincinnamic Aldehyde.

$$C_6H_5-CH\cdot CH_2\cdot CHO$$
$$\quad\quad\quad

Benzoincinnamic aldehyde is easily soluble in hot alcohol, benzene, and acetic acid; in cold ether, chloroform; and insoluble in ligroin (B. P. 40–60°) and water.

Phenylhydrazine and bromine in chloroform solution are without reaction. It was found impossible under any conditions to prepare an oxim. When heated in a sealed tube at 200° with hydroxylamine hydrochloride, alcohol and a small amount of concentrated hydrochloric acid, cinnamic ether and benzil were formed to a small extent. A monoacetyl derivative is described below.

Acetate of Benzoincinnamic Aldehyde $C_{23}H_{19}O_3.CO\,CH_3$.

One molecule of the substance was dissolved in glacial acetic acid and five molecules of acetyl chloride gradually added to the boiling mixture, using a reflux condenser. The boiling was continued for an hour, the mixture cooled, and water added until a cloudiness appeared. In a short time, large glittering crystals separated, which after recrystallization from boiling alcohol melted at 141.5°. The analysis showed it to be a mono-acetyl derivative.

0.2618 grs. gave 0.7467 grs. CO_2 and 0.1366 grs. H_2O.

Found:	Calculated for $C_{25}H_{22}O_4$:
C = 77.40	77.71
H = 5.79	5.69

By saponification with alcoholic-potash the acetyl derivative was reconverted into the original substance, mixed with a small amount of the body, melting at 160–1°.

Constitution of Benzoincinnamic Aldehyde.

Analogy leads us to assign to it the constitutional formula given above. In the absence of a methyl group in the position X, no ring formation can take place. That this formula is correct is shown by the fact that the substance is *easily* oxidized by chromic acid yielding benzil and benzoic acid, while the previously described Δ_2 Keto-R-Hexen derivatives are stable towards oxidizing reagents. The substance does not react with bromine in chloroform solution and distills without decomposition. The presence of the hydroxyl is proven by the formation of the monoacetate, which on saponification reverts to the original substance. As is frequently the case with substances of high molecular weight the presence of the carbonyl groups could

not be demonstrated by the action of phenylhydrazine or hydroxylamine.[14]

Isomer of M. P. 160–1°.

The analysis of the substance melting at 161°, obtained as one of the products of the reaction, shows it to have the same empirical formula as the benzoincinnamic aldehyde.

I. 0.1864 grs. gave 0.5436 grs. CO_2 and 0.1055 grs. H_2O.
II. 0.2744 " " 0.8061 " " " 0.1523 " "

Found:	I.	II.	Calculated for $C_{23}H_{20}O_3$:
C =	79.83	80.12	80.23
H =	6.29	6.16	5.81

As no more than an amount sufficient for the analysis could be obtained from fifteen experiments, the constitution of this substance was not investigated. It is isomeric with benzoincinnamic aldehyde, and probably owes its formation to the transfer of the OH in the CHOH group instead of the transfer of the H. The former reaction is here subordinate, but may yield the principal product as in the following case.

5. ADDITION OF BENZOIN TO BENZALACETOPHENONE.

Under conditions similar to those above benzoin adds itself to benzalacetophenone forming

Iso-benzoinbenzalacetophenone.

$$C_6H_5 - CH - CH\,OH - CO - C_6H_5$$
$$\quad\quad\quad

The substance was recrystallized from boiling alcohol. Then white needles were obtained which melted at 149–150°. This substance was found to the extent of 70 per cent. and is the chief product of the reaction. On analysis figures were obtained agreeing with $C_{29}H_{24}O_3$.

I. 0.3781 grs. gave 1.1481 grs. CO_2 and ——— grs. H_2O.
II. 0.2453 " " 0.7420 " " " 0.1217 " "

Found:	I.	II.	Calculated for $C_{29}H_{24}O_3$:
C =	82.81	82.49	82.85
H =	——	5.51	5.72

The substance is soluble in hot alcohol and acetic acid; in cold benzene, ether, and chloroform. By the action of phenylhydrazine a

Monophenylhydrazone $C_{29}H_{24}O_2 = N.NHC_6H_5$

is formed. Two grams of the substance and 1.4 grams of phenylhydrazine, dissolved in glacial acetic acid, were heated in a water bath for thirty minutes, the whole solidified. The mass was placed on a filter and freed from acids and excess of phenylhydrazine by washing with cold alcohol, dilute hydrochloric acid, and water. After recrystallization from glacial acetic acid crystals were obtained which melted at 210–11°. The substance can be recrystallized from a mixture of benzene and ligroin. The analysis showed it to be a monohydrazone.

I. 0.1295 grs. gave 6.4 cc of nitrogen at 19½° and 744 mm.

Found:	Calculated for $C_{35}H_{30}O_2N$.	$C_{41}H_{36}ON_4$:
N = 5.76	5.66	9.33

The substance is soluble in hot alcohol, acetic acid, benzene, toluene, and chloroform; insoluble in cold alcohol and ligroin (B. P. 40–60°).

Acetyl chloride reacts vigorously with the substance and gives products which are not recrystallizable. Acetic anhydride on the other hand reacts more mildly and forms

Desoxybenzoinstilben.

$$C_6H_5 \cdot CH - CH_2 \cdot C_6H_5$$
$$\quad\quad\quad

yellow color, and evolved carbon dioxide. The solution was cooled and then poured into water to decompose the excess of anhydride. At first an oil separated, which on standing solidified to a mass of large monoclinic crystals. These were further purified by recrystallization from boiling alcohol. The analysis and molecular weight determination showed it to have the formula $C_{28}H_{24}O$.

0.1651 grs. gave 0.5420 grs. CO_2 and 0.0973 grs. H_2O.

Found:	Calculated for $C_{28}H_{24}O$:
C = 89.53	89.36
H = 6.54	6.38

I. 0.2048 grs. gave an elevation of 0.049° in 30.36 grs. of the solvent.
II. 0.3975 " " " " " 0.097° " 30.36 " " " "

Found: I.	II.	Calculated for $C_{28}H_{24}O$:
368.	361.	376.

The substance is soluble in hot acetic acid, benzene, and alcohol in cold chloroform and either. Chromic acid oxidizes it to benzil and some benzoic acid.

Phenylhydrazone of Desoxybenzoinstilben $C_{28}H_{24} : N . NH . C_6H_5$

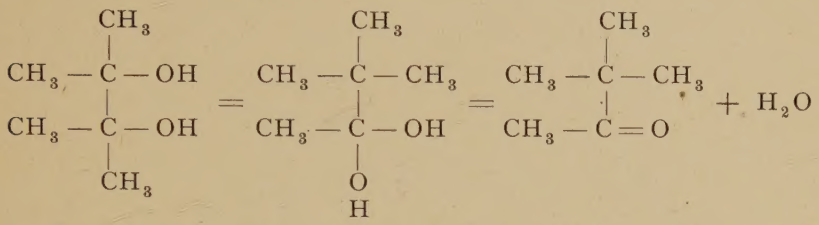
This body is best prepared as follows: Two grams of the substance and excess of phenylhydrazine dissolved in glacial acetic acid are heated on a water bath for two hours. The solution after cooling deposits beautiful white needles. These are filtered off and recrystallized three times from acetic acid. M. P. 212°. On analysis figures were obtained agreeing with $C_{34}H_{30}N_2$.

I. 0.2319 grs. gave 0.7428 grs. CO_2 and 0.1401 grs. H_2O.
II. 0.2269 " " 12.2 cc of nitrogen at 20° and 747 mm.
III. 0.1248 " " 6.7 " " " " 23° " 743 "
IV. 0.2665 " " 14.2 " " " " 16° " 736.7 "

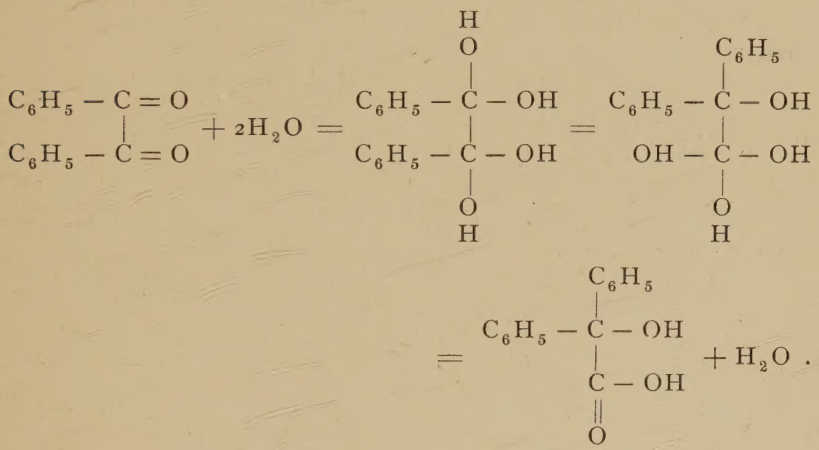
Found: I.	II.	III.	IV.	Calculated for $C_{34}H_{30}N_2$:
C = 87.36	——	——	——	87.55
H = 6.71	——	——	——	6.44
N = ——	6.11	6.05	6.11	6.01

The constitution of desoxybenzoinstilben is clearly established (1) by its oxidation to benzil and some benzoic acid; (2) by its formation of a monohydrazone. The formation of desoxybenzoinstilben from an addition product of benzoin and benzalacetophenone can be under-

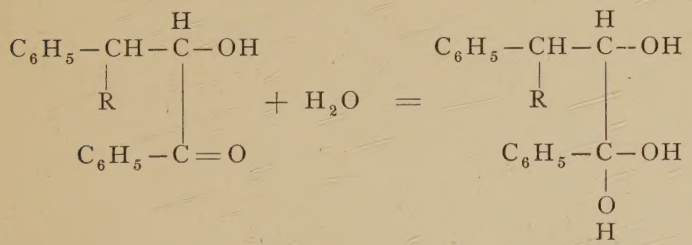
stood only by the assumption that an addition product is formed and by the interchange of the OH in the : CH OH group with C_6H_5. The reaction involved in the formation of desoxybenzoinstilben is similar in character to that which takes place in the change of pinakon into pinacoline:



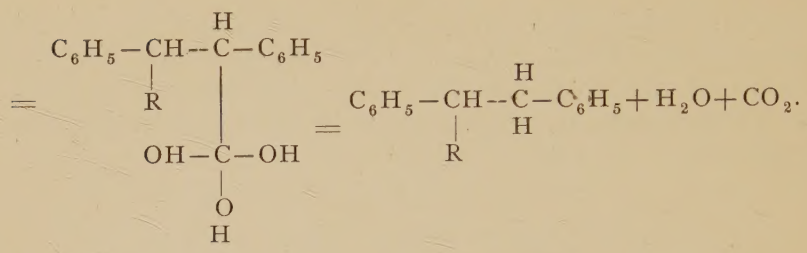
and also in the transformation of benzil into benzilic acid.[15]



The reaction is then represented as follows: (R = desyl)



[15] This explanation of transformation of benzil into benzilic acid was first suggested by Dr. Alex. Smith.



6. BENZOIN AND CINNAMIC ETHER.

Under conditions similar to the above, these substances do not interact. This failure of the benzoin to add itself may be due to the influence of the . $COOC_2H_5$ group, which retards the reactivity of the ethylene grouping. The influence of the .$COOC_2H_5$ group seems to prevent addition whether it is adjacent to the ethylene grouping in the unsaturated substance or adjacent to the : CH OH group of the substance to be added, for mandelic ether does not react with benzalacetophenone. This lack of activity is farther shown in the extreme difficulty with which cinnamic ether absorbs bromine as contrasted with the behavior of cinnamic aldehyde toward the same reagent.

In conclusion I wish to express my most sincere thanks and obligations to Professor Alexander Smith for the many favors which he has shown me, and for his valuable and highly appreciated instruction and hearty coöperation during the work of the present paper.